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## First episode psychosis following receipt of first dose of COVID-19 vaccine: A case report

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### 1. Introduction

COVID-19 still continues to have detrimental effects on mental health of an individual. The mental health impact include the fear of getting infected, fear of spread of infection, social isolation, financial loss and loss of near and dear ones. These issues have further led to new onset or worsening of anxiety, depression, grief, obsessive compulsive disorder, psychosis etc. (Taquet et al., 2021). Amidst all this, COVID vaccine has been introduced across the globe and this has brought relief to a great extent with marked reduction in the infection rates across the globe. However, the acceptability of the vaccine is not universal and many myths have been linked with the vaccine (Lazarus et al., 2021).

Over the period of last few weeks, some of the serious side effects with various COVID-19 vaccines have been documented in the form of Guillain-Barre syndrome (Matarneh et al., 2021). There is limited data with respect to the psychiatric side effects of the COVID-19 vaccine. Few case reports have documented new onset psychosis after the use of messenger-ribonucleic acid (mRNA) based COVID vaccine (Reinfeld et al., 2021; Roberts et al., 2021; Takata et al., 2021; Yesilkaya et al., 2021). Considering the limited data, in this report we present a case of new onset psychosis, following the use of Covishield vaccine [local version of AstraZeneca's Vaxzevria (Adenovirus vector vaccine)].

### 2. Case description

An 18 years old female student, without any past psychiatric (including the substance use disorders) or medical history, with no

family history of mental illness, was brought to the emergency by family members for irrelevant talk and bizarre behavior. There was no past history of physical illness or substance use. Exploration of history revealed that the patient was apparently maintaining well before vaccination and there was no apparent psychosocial stressor prior to vaccination, nor did the patient have any vaccine hesitancy. She received her first dose of the vaccine, and within 2–3 h she developed high grade fever with chills, and multiple episodes of loose stools. The symptoms did not improve with antipyretics. These symptoms were followed by dizziness and one episode of fall; however she did sustain any injury due to the fall. She was taken to local hospital and managed conservatively with intravenous fluids. As per family members fever subsided the next day, but patient reportedly started to remain anxious. She was not able sleep at night, frequently woke-up, appeared fearful and would appear to be staring in between. She would keep on pacing around and would appear distressed. Over the next 3 to 4 days, she started to remain irritable, talk irrelevantly, try to run away from home, voiced delusions of persecution and reference, and reported visual hallucinations of seeing Gods and demons. As it became difficult to control her at home, she was brought to emergency for further management. There was no history of seizures, altered level of consciousness, use of any other medications, depressive features, and neurological deficits.

In the emergency, COVID-19 reverse transcriptase polymerase chain reaction (RT-PCR) was negative. Other investigations revealed presence of pancytopenia and transaminitis. Initially a diagnosis of Post COVID-19 vaccination acute gastroenteritis with pancytopenia and transaminitis was made and psychiatry consultation was sought for her above

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mentioned symptoms. On evaluation, diagnoses of Organic psychosis versus Acute and transient psychosis vs delirium were considered and she was started on Tab. Olanzapine 1.25 mg/day. Further evaluation to rule out other organic causes in the form of blood culture, urine examination including culture, cerebrospinal fluid examination, Wilson disease work-up, evaluation for systemic lupus erythematosus and workup for autoimmune encephalitis did not reveal any abnormality. Electroencephalography (EEG) also did not reveal any abnormality. Magnetic Resonance Imaging (MRI) of brain revealed discrete tiny T2/FLAIR hyperintensities in deep white matter in bilateral fronto-parietal lobes. In view of the absence of inattention and lack of deficits of awareness, and absence of altered level of consciousness, the diagnosis of delirium was ruled out. After excluding other causes and in view of the temporal correlation with the use of Covishield vaccine a diagnosis of vaccine associated psychosis was considered.

In view of the continued symptoms and emergence of catatonia in the form of mutism, staring, rigidity and negativism, she was started on lorazepam 6 mg/day and the dose of olanzapine was slowly increased to 10 mg/day. With this treatment, she showed significant improvement over the period of next 2 weeks and lorazepam was gradually tapered off. She has been maintaining well on this dose for last 3 months, with good adherence and regular follow up. She refuses to take the second dose of COVID-19 vaccine and we have started to reduce the dose of olanzapine and by the last follow-up she was on 1.25 mg/day with no worsening.

### 3. Discussion

There is limited data on association of psychosis with the use of vaccines. There are few case reports of development of psychosis after administration of vaccines for rabies (Bhojani et al., 2014), yellow fever (Romeo et al., 2021), smallpox, typhus and influenza. With respect to COVID-19 vaccine, few published case report has documented the association of psychosis with the use of vaccine and some of the reports indicate that psychosis could be an outcome of autoimmune encephalitis (Reinfeld et al., 2021; Roberts et al., 2021; Takata et al., 2021; Yesilkaya et al., 2021).

Very few reports are available showing COVID-19 vaccine induced psychosis. Studies have shown that SAR-CoV-2 is known to trigger a powerful immune response, which includes the release of large amounts of pro-inflammatory cytokines. It is hypothesized that psychosis may be related to rapid increase in the proinflammatory response and activated autoimmune mechanism (Yesilkaya et al., 2021). The MRI findings of tiny T2/FLAIR hyperintensities in deep white matter in bilateral fronto-parietal lobes in the index case could be indicators of the endothelial and autoimmune activation, as seen in autoimmune encephalitis.

It has also been hypothesized that COVID-19 may increase the risk of psychosis by triggering the cytokine storm. It can be hypothesized that the cytokine storm with elevated serum concentrations of IL-6, IL-8 and IL-2 can affect the levels of monoamine neurotransmitters, i.e., lead to increase reuptake of dopamine, serotonin, and norepinephrine, and influence on the release of neurotransmitters. Cytokines may also result in increased kynurenic acid with resultant NMDA receptor hypofunction, increased pyramidal firing, increased inhibitory activity of the nucleus accumbens, and decreased inhibitory tone over the ventral tegmental area dopaminergic neurons and increased production of dopamine. The increase in the dopamine may be responsible for psychosis.

Schizophrenia has also been related to pro-inflammatory status (Goldsmith et al., 2016). The administration of vaccine elicits an immune response including a cellular immune reaction which leads to T-helper cells production of pro-inflammatory cytokines.

The catatonic features in the index case could be due disruption of the associative functions, especially the connectivity of frontal lobes with parietal cortex and motor areas, contributing to the akinetic form of catatonia (Ellul and Choucha, 2015). Though the risk of developing psychosis after covid vaccine is very rare (Reinfeld et al., 2021), medical professionals need to be sensitized about this for early recognition and benefits of the patient.

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### Contributors

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### Declaration of competing interest

There is no conflict of interest among the authors.

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### References

- Bhojani, S., Aldana-Bernier, L., Sikder, M., Pawelzik, T., 2014. Psychotic disorder after contact with a potentially rabid animal and post-exposure prophylactic anti-rabies treatment. *Clin. Schizophr. Relat. Psychoses* 8, 149–151. <https://doi.org/10.3371/CSRP.BHBE.022213>.
- Ellul, P., Choucha, W., 2015. Neurobiological approach of catatonia and treatment perspectives. *Front. Psychiatry* 6, 182. <https://doi.org/10.3389/fpsy.2015.00182>.
- Goldsmith, D.R., Rapaport, M.H., Miller, B.J., 2016. A meta-analysis of blood cytokine network alterations in psychiatric patients: comparisons between schizophrenia, bipolar disorder and depression. *Mol. Psychiatry* 21, 1696–1709. <https://doi.org/10.1038/mp.2016.3>.
- Lazarus, J.V., Ratzan, S.C., Palayew, A., Gostin, L.O., Larson, H.J., Rabin, K., Kimball, S., El-Mohandes, A., 2021. A global survey of potential acceptance of a COVID-19 vaccine. *Nat. Med.* 27, 225–228. <https://doi.org/10.1038/s41591-020-1124-9>.
- Matarneh, A.S., Al-Battah, A.H., Farooqui, K., Ghamoody, M., Alhatou, M., 2021. COVID-19 vaccine causing Guillain-Barre syndrome, a rare potential side effect. *Clin. Case Rep.* 9, e04756 <https://doi.org/10.1002/ccr3.4756>.
- Reinfeld, S., Cáceda, R., Gil, R., Strom, H., Chacko, M., 2021. Can new onset psychosis occur after mRNA based COVID-19 vaccine administration? A case report. *Psychiatry Res* 304, 114165. <https://doi.org/10.1016/j.psychres.2021.114165>.
- Roberts, K., Sidhu, K., Russel, M., Abbas, M.J., 2021. Psychiatric pathology potentially induced by COVID-19 vaccine. *Prog. Neurol. Psychiatry* 25, 8–10.
- Romeo, B., Rari, E., Mazari, A., Toullec, A., Martelli, C., Benyamina, A., 2021. First-episode psychosis following vaccination against yellow fever: a case report. *Encephale*. <https://doi.org/10.1016/j.encep.2020.09.009>. S0013-7006(21)00021-X.
- Takata, J., Durkin, S.M., Wong, S., et al., 2021. A case report of ChAdOx1 nCoV-19 vaccine-associated encephalitis. *BMC Neurol.* 21, 485.
- Taquet, M., Luciano, S., Geddes, J.R., Harrison, P.J., 2021. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry* 8, 130–140. [https://doi.org/10.1016/S2215-0366\(20\)30462-4](https://doi.org/10.1016/S2215-0366(20)30462-4).
- Yesilkaya, U.H., Sen, M., Tasdemir, B.G., 2021. A novel adverse effect of the BNT162b2 mRNA vaccine: first episode of acute mania with psychotic features. *Brain Behav. Immun. Health* 18, 100363. <https://doi.org/10.1016/j.bbih.2021.100363>.